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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,318	06/23/2008	Stephen J. Klaus	FP0815 US	2668

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EXAMINER	
SPECTOR, LORRAINE	
ART UNIT	PAPER NUMBER
1647	
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06/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,318	KLAUS ET AL.	
	Examiner	Art Unit	
	Lorraine Spector	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 17-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-33* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-16, drawn to a compound that modulates CTGF-mediated cell adhesion,

II. Claims 17-25, drawn to a method of modulating CEGF adhesion,

III. Claims 26, 27 drawn to an *in vitro* assay,

IV. Claims 28-29, drawn to a celular assay,

V. Claims 30-33, drawn to a binding assay for agents that modulating binding of CTGF and HSPG.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: invention I is anticipated by the prior art, for example heparin, (see art rejections below) and therefore cannot form the basis of unity of invention.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Invention I:

A) Applicants are required to elect a monoclonal antibody or a sulfated polysaccharide.

B) Applicants are required to elect a cell selected from a fibroblast, an endothelial cell, or an osteosarcoma cell.

Invention II: Applicants are required to elect a species of disease selected from the group consisting of pulmonary fibrosis, metaplasia, cancer, and diabetic neuropathy.

Invention IV: Applicants are required to elect a cell selected from a fibroblast, an endothelial cell, or an osteosarcoma cell.

Invention V: Applicants are required to elect either beta glycan, or LRP.

The claims are deemed to correspond to the species listed above in the following manner:
Claims 4-5 correspond to a monoclonal antibody or a sulfated polysaccharide.
Claims 8 and 29 correspond to a fibroblast, an endothelial cell, or an osteosarcoma cell.
Claim 24 corresponds to pulmonary fibrosis, claim 223 corresponds to metaplasia and cancer, and claim 25 correaponds to diabetic neuropathy.
Claim 33 relates to beta glycan, and LDL receptor related protein.

The following claim(s) are generic: claims 1-3, 6 and 7 are generic to invention I, claims 17-22 are generic to invention II, claim 29 is generic to invention III, and claims 30-32 are generic to invention IV.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

During a telephone conversation with Christopher Turner on 6/12/2009 a provisional election was made with traverse to prosecute the invention of invention I, claims 1-16, with species elections of sulfated polysaccharide, and fibroblast. Affirmation of this election must be

made by applicant in replying to this Office action. Claims 1-3, and 6-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention or species.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Specification

The disclosure is objected to because of the following informalities: The abbreviation HSPG is not identified anywhere in the specification or claims..

Appropriate correction is required.

Claim interpretation

The claims are drawn to compounds. As such, the methods of using those compounds are given weight in considering enablement, and are only given such weight in considering the prior art as that the compound *could* be used for the recited use, not that it *has* been used that way, nor even that the prior art shows *conception* of using it as recited.

The recitation of "recombinant" CTGF in claim 6 is given no weight, as it is a product-by-process limitation that does not affect the nature of the product itself.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6-7, and 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite as there is no ant4ecedent basis for "the substrate".

Claim 6 is indefinite because it is not clear to what the CTGF is endogenous, and further, because it is unclear what size of the fragments or how many fragments are encompassed.

Claim 7 is indefinite because no species has been specified, such that the metes and bounds of "another species" cannot be determined.

Claim 13 is indefinite because dermatin, chondroitin and heparin are not polysaccharides, they are proteins.

Claims 14-16 are indefinite as it is not clear how one can half-sulfate group per disaccharide.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, and 6-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims read on CTGF from any species. The specification discloses CTGF from human, and mouse (FISP-12). However, this is not sufficiently representative of CTGF from all species, such that the written description does not support the breadth of the claims.

With further respect to claims 9-16, the specification provides no description nor reference to prior art that supports the sulfation of polysaccharides, nor any description of polysaccharides within the metes and bounds of the invention other than dermatan, chondroitin and heparin.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the human and mouse CTGF, the skilled artisan cannot envision the detailed chemical structure of the encompassed CTGF, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid

itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only human and mouse CTGF, dermatan, chondroitin and hepain as the active agents, (and antibodies), but not sulfated forms thereof, nor proteins with altered polysaccharide moieties, and hence the full breadth of the claims does not meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 6, 8, 12, and 13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. There are, of necessity, modulators of CTGF mediated cell adhesion *in vivo*. Accordingly, claims 1, 2, 6, 8, 12, and 13 read on products of nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, and 6-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Grotendorst et al., U.S. Patent Number 5,408,040. See the Detailed description, specifically the following paragraph:

> The invention also discloses a method for ameliorating diseases characterized by a cell proliferative disorder by treating the site of the disease with an effective amount of a CTGF reactive agent. The term "ameliorate" denotes a lessening of the detrimental effect of the disease-inducing response in the patient receiving therapy. Where the disease is due to an overgrowth of cells, an antagonist of CTGF polypeptide is effective in decreasing the amount of growth factor that can bind to a CTGF specific receptor on a cell. Such an antagonist may be a CTGF specific antibody or functional fragments thereof (e.g., Fab, F(ab').sub.2). The treatment requires contacting the site of the disease with the antagonist. Where the cell proliferative disorder is due to a diminished amount of growth of cells, a CTGF reactive agent which is stimulatory is contacted with the site of the disease. For example, TGF-.beta. is one such reactive agent. Other agents will be known to those skilled in the art.

Therefore, Grotendorst et al. disclose an antibody that clearly anticipates the claims.

Claims 1-3, and 6-16 are rejected under 35 U.S.C. 102(b) as being anticipated by 6,388,060 (Gao et al.).

The patent is drawn to over-sulfated polysaccharides. At column 11, line 63, for example, it is disclosed that oversulfated heparin with 3.35 sulfates/disaccharide were produced. Over-sulfated dermatin sulfate is also disclosed, see claim 10.

Polysaccharides are defined as comprising more than 10 monosaccharides that are linked by means of glycosidic linkages. (col. 1, beginning at line 44). Heparanoides are defined as having at least 18 different disaccharides (paragraph bridging cols. 3-4). It is noted that CTGF comprises fragments of CTGF (see claim 7). With respect to the limitations of claim 12, as claim

13 is presumed to be properly limiting, the glycosylation patterns are taken to be inherent to the molecules.

Accordingly, the claims are anticipated by Gao et al.

Double Patenting

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday from 9-5, and Tuesday, Thursday and Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Manjunath Rao, at telephone number 571-272-0939.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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